UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF WISCONSIN

ILLUMINA, INC.,

Case No.: 09-cv-277-bbc
09-cv-665-bbc

Plaintiff,

v.

AFFYMETRIX, INC.,

Defendant.

EXPERT REPORT AND DECLARATION OF DR. MILAN MRKSICH ON INFRINGEMENT

I, Dr. Milan Mrksich, hereby make the following disclosure pursuant to Fed. R. Civ. P. 26(a)(2):

I. INTRODUCTION

1. I have been retained by the firm of Foley & Lardner LLP, who represent Plaintiff Illumina Incorporated in this case, as an expert regarding technical issues in this case, including the design, preparation and use of oligonucleotide arrays of arrays. My curriculum vitae is attached in Exhibit A, which includes all publications I authored in the previous 10 years.

2. I have been asked to express an opinion on whether the accused products (discussed more specifically below) of Defendant Affymetrix fall within certain claims of U.S. Patent Nos. 7,510,841 ("the '841 patent") and 7,612,020 ("the '020 patent").

3. I am currently serving as an expert witness only in this case. I have not testified at trial or deposition in connection with any other matter during the last four years.

4. I am being compensated at the rate of $500.00 per hour for time spent working on issues in this case. I will be compensated at the rate of $600.00 per hour for time spent testifying.

My compensation is not dependent on or related in any manner to the outcome of the current litigation. I have no financial interest whatsoever in the outcome of the litigation.

II. QUALIFICATIONS

5. I attended the University of Illinois in Urbana-Champaign, Illinois from 1986 to 1989, and received a Bachelor of Science degree in Chemistry, *magna cum laude* in 1989. I received my Ph.D. in Organic Chemistry from the California Institute of Technology in 1994. My thesis research involved the design, synthesis and characterization of small molecules that bind to DNA in a sequence specific manner.

6. From 1994 to 1996, I was an American Cancer Society Postdoctoral Research Fellow at Harvard University. At Harvard, my research was directed towards the development and application of surface chemistries for controlling the interactions of biomolecules and cells with materials and for applications in biosensors. This work included the development of methods for patterning the immobilization of bioactive agents on surfaces and the construction of arrays.

7. In 1996, I became a faculty member of the Department of Chemistry at The University of Chicago. I currently hold the position of Professor of Chemistry and am a member of the Institute for Biophysical Dynamics. Since 2001, I have also served as the Associate Director of the Nanoscale Science and Engineering Center at Northwestern University.

8. Since 1996, my research has focused on the intersection of chemistry, biology and materials. A common theme in my research programs is the control of interfaces between a material and a biological fluid. My research program makes use of self-assembled monolayers to design and synthesize surfaces having well-defined structures and properties. Research activity in my group can be divided into three general areas.

9. The first program develops technologies for using arrays to assay biochemical activities. My research group has developed methods for preparing arrays of bioactive molecules, including peptides, proteins, oligosaccharides, nucleic acids and other classes of molecules. Our strategies have used both photolithographic and robotic methods and have made extensive use of self-assembled monolayer chemistries to control the activities and densities of biomolecules in features of the array. We have also developed a label-free technology based on mass spectrometry to analyze the arrays after they have been treated with samples. We have published more than twenty papers that describe the application of this 'SAMDI' format to assays of a broad range of enzyme activities, protein-binding activities, and nucleic acid hybridization. We have also adapted this method for applications in high throughput screening, which requires that many assays be performed in parallel.

10. The second research program addresses the adhesion and migration of cells. In the body, cells are attached to an insoluble matrix and both the adhesion of cells and the functions of the cells are regulated by ligand-receptor interactions between the cell and the underlying matrix. We prepare surfaces that are modified with peptides, proteins and carbohydrates and that serve as mimics of the natural matrix, and we use these model surfaces to understand the roles that designated ligand-receptor interactions play in mediating cell adhesion and other cellular functions. Our work has identified ligands that mediate the adhesion of cells and has framed new opportunities for treating a variety of diseases, including cancer and thrombosis.

11. A third research program seeks to control and understand the interfaces between materials and biological fluids. Such interfaces are prevalent, including substrates used in tissue culture, biochip microarrays used in genotyping or gene expression analysis, and microfluidic devices used in biochemical assays. This work is highly relevant to the design of surfaces that are

employed in biosensors. In particular, my program develops surface chemistries that give high discrimination for detecting specific biological analytes in samples that contain many components.

12. Since 1996, I have served on the Defense Sciences Research Council. I served as the Chairman of this group from 2006-2008. This Council is a technical advisory board to the Defense Advanced Research Projects Agency of the Department of Defense. In this capacity, I have organized and participated in studies on a broad range of technical subjects, including sensors for detecting chemical and biological warfare agents. I have also served on the Board of Governors for Argonne National Laboratory for a period of six years.

13. I am currently a member of the Scientific Advisory Boards of three biotechnology companies and within the past ten years have served on the Advisory Boards of four other biotechnology companies. These companies were engaged in programs to commercialize a variety of biochemical technologies, including novel pharmaceuticals, bioactive arrays for parallel assays, high throughput and high content screening methods used in the pharmaceutical industry, and high throughput methods for sequencing DNA. My role with each of these companies has included advising on the development and use of surfaces that interact with biological species, on methods used to create arrays of bioactive molecules, on the development of assay formats for particular classes of analytes and samples, and on applications of these technologies.

14. I routinely review scientific papers that have been submitted for publication. In the past decade, I have reviewed more than 400 manuscripts for journals including *Science*, *Nature*, *Advanced Materials*, *Nature Biotechnology*, *Journal of the American Chemical Society*, and *Trends in Biotechnology*. I am a member of the Editorial Advisory Board for the journals *Langmuir*, *E-Biomed: The Journal of Regenerative Medicine*, *IEEE Transactions on NanoBioscience*, *Chemistry & Biology*, and *Small*.

15. I have served on several Biosensor Advisory Panels. The appointments include service as the Co-Chair of the National Institutes of Health Symposium on Biosensors in 2001 and as the Vice-Chair of the World Technology Evaluation Center Panel for International Research and Development in Biosensing in 2002-03. The latter activity was sponsored by the National Science Foundation, the National Institutes of Health, the United States Department of Agriculture, NASA, and the Army Research Office to assess and compare the state of research and development of biosensors in the United States, Europe and Japan. The state of the art in DNA arrays was an important technology considered in each of those activities.

16. I have also served as a member of a panel to evaluate research proposals submitted to the National Institutes of Health. This panel reviews proposals in the broad area of biosensor research and development, including proposals directed towards the design, preparation and application of oligonucleotide arrays.

17. I am the author or co-author of more than 130 technical papers. Furthermore, I am a named inventor on 10 issued U.S. patents and 16 published patent applications.

18. I have taught approximately 25 courses at the University of Chicago at both undergraduate and graduate levels. The undergraduate courses included those in general chemistry, organic chemistry and biochemistry. The graduate courses included those in biochemistry, chemical biology, high throughput and genomic assays, biomaterials and organic chemistry.

19. I have presented more than 200 invited lectures in the past ten years, including many international lectures.

20. I have received several awards that recognize my technical contributions. These awards include the American Chemical Society Arthur C. Cope Young Scholar Award in 2003, the TR100 Young Innovator Award in 2002, and the Camille Dreyfus Teacher-Scholar Award in 2000.

III. MATERIALS REVIEWED

21. In my study of this matter, I have reviewed the materials as set forth in Exhibit B.

22. I have been advised by counsel for Illumina that discovery in this case has not been completed. Therefore, my investigation and review in this matter is ongoing. Additional information may become available which would further support or modify the conclusions that I have reached to date. Further, I reserve the right to consider and comment on any additional expert statements and testimony of Affymetrix experts in this matter. Any changes or necessary amplification of these conclusions will be addressed in supplemental reports or testimony, which I reserve the right to provide. I also reserve the right to rely on demonstrative exhibits to explain and supplement my testimony at trial.

23. I have reviewed the Court's July 17, 2010 Opinion and Order regarding claim construction and have applied the Court's claim construction in my analysis. I reserve the right to amend or supplement my analysis in the event the Court modifies or supplements its claim construction.

IV. SCOPE OF ASSIGNMENT

24. Although I am not a lawyer, I have been advised that Illumina initiated this action seeking, among other things, a judgment that certain of Affymetrix's products (or use of such products) infringe the '841 and '020 patents. This report provides certain technical information regarding the design, preparation and use of DNA arrays, including the related array of arrays, and addresses whether Affymetrix's products meets certain limitations found in the claims of the '841 and '020 patents.

25. The '841 patent has 27 claims and the '020 patent has 76 claims. I understand from counsel for Illumina that, in this matter, Illumina is currently asserting that Affymetrix's products are

covered by claims 1, 2, 3, 8, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21, 24, 25 and 26 of the '841 patent and 1, 3, 4, 7, 9, 11, 16, 18, 19, 20, 21, 24, 26, 28, 33, 34, 35, 36, 37, 40, 42, 44, 49, 50, 51, 52, 55, 57, 59, 63, 64, 66, 69, 71, 73 and 76 of the '020 patent. Accordingly, I have limited my analysis in this report to the question of whether products marketed by Affymetrix (or use of such products) meet the limitations of these claims. I reserve the right to opine on additional claims that Illumina may assert.

26. I have reviewed and incorporate by reference the claim charts in Illumina, Inc.'s Supplemented Responses to Affymetrix, Inc.'s First Set of Interrogatories (Nos. 1-8), dated September 1, 2009, and Illumina, Inc.'s Responses to Affymetrix, Inc.'s Second Set of Interrogatories (Nos. 9-16), dated April 30, 2010.

27. Although I am not a lawyer, I have been advised that literal infringement of a claim requires practicing each and every step or limitation of the claim. I have also been advised that infringement of a claim under the doctrine of equivalents requires components or steps that are identical or equivalent to the requirements of the claim. I further understand that claims are interpreted from the viewpoint of the person of ordinary skill in the art.

28. In defining "one of ordinary skill in the art," I have been advised to consider factors such as the educational level and years of experience not only of the person or persons who have developed the invention that is the subject of the case, but also of others working in the pertinent art at the time of the invention; the types of problems encountered in the art; the teachings of the prior art; patents and publications of other persons or companies; and the sophistication of the technology. I further understand that one of ordinary skill in the art is presumed to think along conventional lines without undertaking to innovate. I understand that a person of ordinary skill in the art is not a

specific real individual, but rather a hypothetical individual having the qualities reflected by the factors discussed above.

29. I have assessed the level of ordinary skill in the art based upon my fifteen years of teaching students in chemistry and biology, advising companies and governmental organizations that develop or use biosensors and arrays, and first-hand experience in biosensor and array research. In the course of my professional activities, I have followed the research and development of DNA arrays since the mid-1990s and have been directly involved in research to develop and apply arrays since that time.

30. In order to determine who "one of ordinary skill in the art" is I found it essential to first define what that "art" is. It is my understanding that the "art" is designing, preparing and using DNA arrays, including an array of arrays. In my opinion, one of ordinary skill in this art in the mid-to-late 1990s, and particularly in 1998, would have acquired 1-2 years of experience in an academic, government or industrial research laboratory that is concerned with biological arrays. Further, one of ordinary skill in the art would have earned at least a college-level degree in one of the following fields: chemistry, biochemistry, materials science or bioengineering. Preferably, one of ordinary skill in the art would have a general knowledge of DNA assays, surface modification, fluorescence detection, integration, and further would have a detailed knowledge in at least one of the preceding technical areas. In conducting my analysis, I have adopted the view of one having ordinary skill in the art at the time of the invention.

V. DNA ARRAYS IN GENERAL

31. The following background information concerning the development and application of DNA arrays is based upon my reading of various patents and articles and from my first-hand knowledge of the topic.

32. DNA is the molecule that carries the genetic code, or blueprint, for life. DNA is made from two molecules that resemble strands and that pair with one another to give a structure that resembles a twisted ladder, or a helix and which is also known as a 'duplex'. Each strand is a made by arranging four types of building blocks in a linear arrangement. For DNA, the building blocks are nucleotides, or 'bases', that are known as 'A', 'T', 'G' and 'C'. The particular ordering of these bases represents a 'sequence' of DNA. For example, a DNA molecule can contain the sequence 5'-AGGCTAAGCTAG-3', where the 5' and 3' terms indicate the orientation of the strand. Two strands are joined together, or hybridized, in an anti-parallel orientation. The two strands are held together through the interactions of pairs of bases, or 'base pairs', where one partner of each pair is present on each strand.

33. The pairing of bases is specific. A pairs with T and G pairs with C, but the other combinations of bases (i.e., A and G) do not form stable base pairs. The A-T and G-C base pairs are referred to as 'stable base pairs' and the other base pairs are referred to as 'unstable base pairs'. In this way, the formation of A-T and G-C base pairs allows two DNA molecules to associate with each other to form a DNA double helix. It follows that two strands will hybridize if their sequences are 'complementary' in that stable base pairs are formed along the helix. For example, a DNA molecule having the sequence 5'-GGCATTACGCAATG-3' will hybridize with a second DNA molecule having the sequence 5'-CATTGCGTAATGCC-3', but not with a DNA molecule having the sequence 5'-CATTGCGTTATGCC-3'.

34. RNA is an analog of DNA that plays a role in gene expression. A gene is a sequence of DNA that carries the code for the synthesis of a particular protein. Genes must be 'expressed' in order to enable the synthesis of their protein products. When activated, the DNA in the nucleus is copied into a complementary RNA strand, which is also known as mRNA, and which then exits the

nucleus and serves as an instruction to the ribosome to make a protein of the designated sequence. Hence, the presence of mRNA in the cell is associated with expression of the relevant gene.

35. RNA is made up of four nucleoside bases, which are 'A', 'U', 'G' and 'C'. These bases differ from those present in DNA in that the U base in RNA substitutes for the T base in DNA. One strand of DNA and one strand of RNA can pair to make a helix, where A pairs with U, G pairs with C, C pairs with G and T pairs with A, and where the first base in each pair is present on the DNA molecule and the second base is present on the RNA molecule.

36. Oligonucleotides are short single-stranded DNA molecules, which typically include from 5 to 100 bases. Oligonucleotides are frequently made in the laboratory using synthetic methods. Two oligonucleotides are capable of hybridizing to give a short DNA duplex. A DNA duplex that is formed from the hybridization of two oligonucleotides such that each base on each strand participates in a base pair and wherein each base pair is either a A-T or G-C pair is referred to as a 'perfectly matched' duplex. A DNA duplex that is formed from the hybridization of two oligonucleotides such that other base pairs are present (for example, A-G or C-A) is referred to as a 'mismatched' duplex.

37. In general, the tendency of two oligonucleotides to hybridize increases with the length of the sequences that assemble into a double stranded DNA. That is, a perfectly matched duplex that has 20 base pairs will in general form more readily and be more stable than a perfectly matched duplex that has 15 base pairs. The G-C base pair is more stable than the A-T base pair and for that reason a perfectly matched duplex of a defined length will generally have greater stability as the fraction of G-C base pairs is increased. Finally, the inclusion of unstable base pairs in a duplex will decrease the stability of the duplex relative to the same duplex having all stable base pairs. Hence,

the stability of a hybridized duplex will depend on length, sequence, and the proportion of stable and unstable base pairs.

38. The ability of two strands of DNA to hybridize to form a duplex also depends on the hybridization conditions. For example, the tendency of two strands to hybridize is increased at lower temperature and is decreased at higher temperature. Further, the tendency of two strands to hybridize depends on the composition of the solution in which hybridization occurs. The composition can be varied by changing the type and concentrations of salts and ions, adjusting the pH, using mixtures of solvents, and through the addition of other molecules to the solution. These parameters can be adjusted and controlled to provide for defined hybridization conditions that provide for the hybridization of DNA or RNA strands in a particular experiment.

39. The conditions can be further optimized to promote the hybridization of DNA and RNA strands that are perfectly matched while at the same time minimizing the hybridization of DNA and RNA strands that would include an unstable base pair in the duplex. Hybridization conditions that satisfy this condition are referred to as ‘stringent’ hybridization conditions.

40. Stringent hybridization conditions can be used to identify an oligonucleotide of unknown sequence. Under stringent hybridization conditions, two oligonucleotides will hybridize only if their sequences are perfectly complementary. If two oligonucleotides hybridize under these conditions and if the sequence of the first oligonucleotide is known and the sequence of the second is partially or completely unknown, then the sequence of the second oligonucleotide can be deduced. This ability to identify the sequence of the second oligonucleotide follows from the complementarity of two strands in a perfectly matched duplex. For example, where the first oligonucleotide has a T base, the second oligonucleotide will have an A base, and where the first has a G base, the second will have a C base. By knowing that only A-T and G-C base pairs are present in perfectly matched

duplex, the sequence of the second oligonucleotide can be directly determined from knowledge of the sequence of the first oligonucleotide.

41. This principle can be used to design a test for the presence of a DNA molecule having a designated sequence. In a hypothetical example, consider a target analyte having the sequence 5'-GTTACA-3'. This oligonucleotide would form a perfectly matched duplex with a second oligonucleotide having the sequence 5'-TGTAAC-3', but not with any other oligonucleotide that did not have this sequence. Hence, combining the target analyte with the second oligonucleotide under stringent hybridization conditions will lead to the formation of a duplex. The following experiment can be used to test for the presence of the target analyte in a sample. The second oligonucleotide (with sequence 5'-TGTAAC-3') is added to the sample that may or may not contain the target analyte and the conditions are adjusted to achieve stringent hybridization conditions. The solution is then tested for the presence of a duplex DNA. If the duplex DNA is present, then the target analyte is present in the sample. Conversely, if duplex DNA is not present, then the target analyte is not present in the sample. This example illustrates the concept for using a 'hybridization assay' to detect a DNA or RNA strand having a designated sequence.

42. One common format for performing a hybridization assay involves attaching the second sequence to a solid surface and applying to the surface a sample that is to be tested for the presence of the target analyte. The sample is kept in contact with the surface under stringent hybridization conditions and the surface is then analyzed to detect the presence of the target analyte at the surface. In this format, the oligonucleotide that is attached to the surface is known as the 'probe' strand and is chosen to have a sequence that is complementary to that of the target analyte, and which therefore will form a perfectly matched duplex with the target analyte. The length of the probe strand is typically between 15 and 30 nucleotides and depends on the particular application.

43. Detection of the target analyte is most commonly performed using an optical label. For example, the target analyte can be prepared in such a way that it has attached to it a molecule that has a unique optical signature. Following hybridization of the target analyte to the probe strand on the surface, the surface can be analyzed to measure the optical signature and therefore to determine whether the target analyte has hybridized to the probe strand. In another example, the target analyte in the sample will hybridize with the probe strand on the surface, and then a subsequent protocol is used to introduce a label onto the hybridized duplex. The presence of the label, and therefore of the target analyte in the sample, can then be determined by detecting the unique optical signature of the label.

44. The most common methods use optical labels that are fluorescent. The molecules that are used as fluorescent labels are referred to as ‘fluorophores’, ‘fluorescent molecules’, or ‘fluorochromes’. A fluorescent molecule interacts with light of a certain wavelength to give an ‘excited state’ of the molecule, which then emits light at a slightly longer wavelength and returns to its initial state or ‘ground state’. Light is an electromagnetic wave that is characterized by its wavelength. Different colors of light have distinct wavelengths. For example, red light has a wavelength of approximately 650 nanometers (nm) and blue light has a wavelength of approximately 475 nm. Similarly, a rainbow represents a separation of white light into its component colors. Light of shorter wavelength is more energetic than light of longer wavelength. The specific wavelengths of light at which a fluorescent molecule is excited and which is emitted from the molecule are unique to each molecule, and represent a unique optical signature for that molecule. Instruments that are used to detect the presence of a fluorescent molecule are engineered to use light of the appropriate wavelength to analyze the molecule and a detector having the appropriate properties to analyze the appropriate wavelength for the emitted light.

45. The preceding discussion illustrates the basis for an 'assay', or test, to determine the presence of a DNA or RNA target analyte in a sample. For example, a surface is prepared that has attached to it a probe oligonucleotide that is complementary to the sequence of the target analyte. The sample is introduced onto the surface under stringent hybridization conditions. The sample is either prepared so that the target analyte is directly labeled with a fluorophore or is modified to permit a subsequent treatment to introduce a fluorophore. That is, the fluorophore can be attached to the target analyte or probe strand afterwards if a duplex has formed between the target analyte and the probe strand. The surface is then analyzed with an instrument to detect the unique optical signature of the fluorophore. Detection of the signal is evidence that the target analyte is present in the sample, and quantitation of the signal can be used to determine the amount of target analyte in the sample. Similarly, a lack of signal for the fluorophore is evidence that the target analyte is absent in the sample.

46. A benefit of assays that use a probe oligonucleotide that is attached to a surface, as described above, is that the assay can be 'multiplexed' to individually detect the presence or absence of many target analytes in the same sample. For example, a sample can be analyzed for the presence of two different target analytes by performing two separate assays as described above, wherein the first assay would use a surface having attached to it a probe strand that is complementary to the first target analyte and the second assay would use a surface having attached to it a probe strand that is complementary to the second target analyte. But the two assays could be performed using a single surface that has two regions on it, wherein the first region has attached to it the first probe strand and the second region has attached to it the second probe strand. Treatment of the surface with a sample under stringent hybridization conditions will then lead to hybridization of the first target analyte, if present in the sample, to the first region and will similarly lead to hybridization of the second target

analyte, if present, to the second region. The surfaces then have to be analyzed with an instrument that can resolve the unique optical signature that is present at each of the two regions. In this way, both assays are performed simultaneously and therefore require less total sample and less time to perform the two assays.

47. The strategy for multiplexed assays described above can be extended to surfaces that are suitable for the simultaneous detection of much larger numbers of target analytes. For example, a surface can be prepared so that there is a ten by ten array of regions, to each of which is attached a probe strand that is complementary to a different target analyte. Such a surface could be used to analyze for the presence or absence of one hundred unique target analytes in a sample. By similar logic, a surface having millions of regions could be used to analyze a sample for the presence or absence of massive numbers of target analytes.

48. Such surfaces that comprise large numbers of regions, each of which have attached to them a distinct probe oligonucleotide, are commonly referred to as ‘gene chips’, ‘DNA arrays’, or ‘oligonucleotide arrays’. They can be prepared by first synthesizing the probe oligonucleotides using standard solid-phase synthetic methods, and then attaching the probes to a surface such that each distinct probe is attached to a distinct region on the surface. There exist a wide variety of surface chemistries and attachment chemistries that can be used to perform this step. At the time of the invention, this method was known, but in practice the expense associated with synthesizing and purifying large numbers of oligonucleotides, and the challenges associated with applying large numbers of probes to designated regions on a surface, both limited the utility of this approach.

49. An alternative method for preparing the gene chips relies on the step-wise synthesis of the probe oligonucleotides directly on the surface. In this method, referred to as photolithography, light is used to activate designated regions on the surface for attachment of bases. In one example,

the method starts with a surface that is modified with a photoprotecting group. The surface is covered with a 'mask' and irradiated with light, such that the surface is exposed to the light only at those regions where the mask allows the light to pass through, but not at the regions where the mask blocks the path of the light. Where the surface is exposed to the light, the photoprotecting group is removed, which then results in activation of the molecules on the surface for attachment of a base. The base itself is modified with a photoprotecting group so that it can later be exposed to light to activate the molecule for attachment of another base. In this way, a series of masks that direct which regions on the surface are exposed to light is used to perform cycles of synthesis, and ultimately lead to the preparation of an oligonucleotide array.

50. The density of oligonucleotides within a region is an important parameter that affects the quality of the assays that are used to detect the presence or absence of target analytes. Densities of probe that are less than the optimum density will limit the amount of target strand that can hybridize with the probe, and therefore will limit the intensity of the optical signal that is detected from the fluorophore and consequently will limit the sensitivity of the assay. Densities of probe that are greater than the optimum density will lead to probes that are crowded on the surface and which may interfere with the hybridization of target analytes with probe strands on the surface. For these reasons, it is important to optimize the density of the probe on the array and to establish technical protocols for controlling the density and for ensuring the quality of gene chips that are manufactured.

51. Photolithographic methods are inherently limited in that they cannot be used to create regions that have a constant density of probe oligonucleotide throughout a region on the array. When the surface is exposed to light, the amount of photoprotecting group that is removed, or the yield, is dependent on the intensity of the light that irradiates the surface. Because of imperfections in optics and because of diffraction of light near the edges of the transparent regions of the mask, a region on

the surface is exposed to a variable intensity of light and therefore gives variable removal of the protecting group and a variable density of the probe oligonucleotide. Commonly, the density of a probe within a region is maximal near the center of the region, is reasonably uniform in the area near the center, and then decreases near the perimeter of the region. Hence, the center of the region or feature will generally have the desired oligonecleotide attached to it. However, for the area near the edge of the feature the fraction of the total oligonucleotides that is the desired sequence will be lower. The fraction of incorrectly constructed oligonucleotides is expected to be the greatest at the border between two adjacent features.

52. Because of the non-uniformity of the probe density within a particular region, the instruments and data processing methods that are used to analyze oligonucleotide arrays do not collect and process the optical signal that is present in the entire region. Instead, only the signal from a fraction of the region is used to detect the presence or absence of a target analyte in a sample. Typically, the area of the region that is analyzed represents the center area of the region.

53. Oligonucleotide arrays are used for many applications. One common application is in the determination of the global gene expression profile for a cell culture or biological tissue. In one example, a standard protocol is used to collect mRNA from a population of cultured cells. The mRNA is processed to generate RNA fragments that are labeled, either with a fluorophore or a molecule that can later be used to attach a fluorophore to the hybridized duplex on the surface. The sample is then applied to an oligonucleotide array, where the RNA fragments are allowed to hybridize with probe oligonucleotides in the array, and the array is then analyzed to detect the unique optical signature of the label at each site. Because the presence of mRNA is associated with the expression of a unique gene, this experiment can report on the expression of each of nearly all genes that are present in the genome. In a related example, two distinct cell populations can be processed

such that the RNA from one is labeled with one fluorophore and the RNA from the second is labeled with a second fluorophore. The two samples are then mixed and applied to the array. In this way, if both cell populations were expressing a certain gene, the RNA that derives from that gene expression event will contain both labels. The array is imaged to determine the ratio of the two fluorophores at each site. This information is used to characterize the relative amounts of expression of each gene in the two samples.

54. Another common application of oligonucleotide arrays is directed towards genotyping. Each person's DNA is highly similar, but differs at key locations in the sequence. It is these differences that determine an individual's traits, including physical features and predisposition to future disease. One type of difference is known as a single nucleotide polymorphism, or SNP. A SNP is a difference where a single nucleotide in a DNA sequence differs between individuals. In many cases, only two forms of the DNA sequence are known—again, where the sequences differ at a single nucleotide position—and therefore assays are used to determine whether a specific individual has the first or the second 'allele'. An oligonucleotide array that contains distinct probe oligonucleotides that are complementary to each of the two alleles can then be used to determine which allele a specific individual has. In cases where these alleles correlate with a greater or lesser risk for developing a disease, the information provided in the assay can be important for closer monitoring to detect the onset of an early stage of disease in an individual. The oligonucleotides can also be used to analyze for so-called 'indels', which represent a DNA sequence that differs from a first DNA sequence in that it has a base either inserted or deleted from the first sequence.

55. In the late 1990's, the oligonucleotide array art was still in its early development and the use of an oligonucleotide array to perform an analysis of genomic DNA was still an expensive and time-consuming experiment. Hence, the throughput of the analysis was slow and it was not yet

routine for investigators to perform many analyses. At that time, the oligonucleotide arrays mainly found applications in the research arena and had not yet become common for analyzing genomic DNA for diagnostic or genotyping applications.

56. The 'array of arrays' concept described in the patents-in-suit was significant to improving the throughput and reducing the time and expense of gene chip experiment. An array of arrays refers to the use of multiple copies of an oligonucleotide array—where the arrays could either be identical or different, depending on the application—so that multiple assays could be performed in the time that a single assay was commonly performed. Typically, a substrate that was prepared to contain an array of arrays would be treated with samples such that each individual array was exposed to a distinct sample. Because each array was simultaneously exposed to the samples, many array experiments could be performed in the time that was required to perform a single experiment when using a single array. Further, the miniaturization of the arrays meant that smaller sample volumes could be analyzed, which increased the throughput with which samples could be processed to generate the target analytes that are applied to the surfaces.

VI. DEVELOPMENT AND PATENT HISTORY OF THE ARRAY OF ARRAYS CONCEPT

57. In his deposition in connection with this matter, Dr. Goldberg discussed Affymetrix's product development efforts for the peg array products. Specifically, Affymetrix had investigated a number of concepts for high throughput applications of the gene chip technology. Affymetrix had started discussions and development work on the peg array concept in the 2002 timeframe, and this work led to the array of arrays products that are now marketed by Affymetrix, including the GeneTitan instrument and the Plate Array products. Those products were introduced in the 2008 time frame. See Goldberg Deposition, pp. 23-24 and 151.

58. Illumina had begun working on the array of arrays concept for product development in the 1998 time frame. A description of Illumina's concepts and understanding of this technology is found in a patent application that was filed in 1998. The patent applications for the patents-in-suit refer to 'composite arrays' which I find to be generally synonymous with the array of arrays concept. Illumina was marketing products that incorporated the 'array of arrays' concept in 2001. See ILL2938265-2938321.

59. United States Patent No. 7,510,841 ("the '841 patent"), entitled "Methods of Making and Using Composite Arrays for the Detection of a Plurality of Target Analytes," was filed on January 28, 2004 and issued on March 31, 2009. The patent claims priority to a provisional application that was filed on December 28, 1998. Mark Chee, John Stuelpnagel, and Steven Auger are the named inventors of the patent. The primary examiner at the United States Patent and Trademark Office that examined the patent was Kenneth R. Horlick and the assistant examiner was Molly R. Baughman. The references listed on the first four pages of the patent were considered by the examiners during prosecution.

60. United States Patent No. 7,612,020 ("the '020 patent"), entitled "Composite Arrays Utilizing Microspheres with a Hybridization Chamber," was filed on January 28, 2004 and issued on November 3, 2009. The patent claims priority to the same provisional application that was filed on December 28, 1998. Mark Chee, John Stuelpnagel, and Steven Auger are the named inventors of the patent. The primary examiner at the United States Patent and Trademark Office that examined the patent was Amber D. Steele. The references listed on the first four pages of the patent were considered by the examiner during prosecution.

61. Figure 1B of the patents in suit is shown below. The first substrate, which is identified by the number 40 in the figure, can be a standard 96-well microtiter plate. The second

substrate is identified with the number 10 in Fig. 1B, and includes an array of pegs or projections that are identified by the number 20. Each of these projections includes an array of bioactive agents (including, for example, DNA) that are directly coupled to the pegs. These fragments of DNA are the probes that bind to the target analytes. The array of DNA probes can be prepared using a process based on photolithography. See '841 patent, col. 5: lines 3-9.

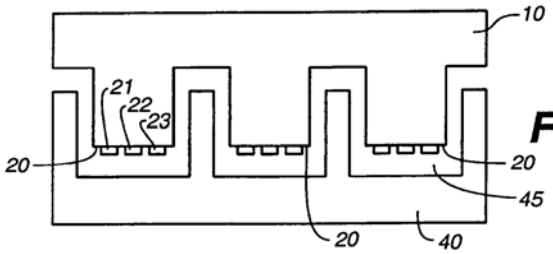

FIG._1B

62. The '841 patent claims methods for making and using an array of arrays for the simultaneous processing of a number of samples. The method entails the use of a substrate having a plurality of assay wells, each of which contains a sample having a plurality of target analytes. Further, the method entails the use of a second substrate that has a plurality of projections that each contains an array of different bioactive agents. The second substrate is inserted into the first such that each projection is inserted into a unique sample of the first substrate under conditions that are suitable for the binding of target analytes to bioactive agents in the array. The arrays are then analyzed to detect the presence or absence of the target analytes.

63. The '841 patent contains one independent claim:

> 1. A method of detecting the presence or absence of different target analytes, comprising:
>
> (a) providing a first substrate with a surface comprising a plurality of assay wells, wherein said assay wells contain sample solutions each having a plurality of target analytes;
>
> (b) providing a second substrate comprising a plurality of array locations, each array location

> comprising a plurality of discrete sites on a projection, wherein said sites comprise different bioactive agents;
>
> (c) dipping the projections of said second substrate into said assay wells such that each array location of said second substrate contacts sample solution in a different well of said first substrate under conditions suitable for binding of said different target analytes to said different bioactive agents, thereby processing said sample solutions in parallel; and
>
> (d) detecting the presence or absence of said target analytes.

64. The ‘020 patent is closely related to the ‘841 patent and claims the array of arrays that are used in the ‘841 patent. The ’020 patent contains five independent claims: 1, 20, 36, 51 and 64:

> 1. An array of arrays comprising:
>
> (a) a first substrate with a surface comprising a plurality of assay wells comprising samples; and
>
> (b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and wherein said first substrate and said second substrate are arranged such that projections of said second substrate are fitted into assay wells of the first substrate.
>
> 20. An array of arrays comprising
>
> a plate having wells and a substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and wherein projections of said substrate are fitted into wells of said plate.
>
> 36. An array of arrays comprising:

(a) a first substrate with a surface comprising a plurality of wells; and

(b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and wherein projections of said second substrate are fitted into wells of the first substrate.

51. An array of arrays comprising:

(a) a first substrate with a surface comprising a plurality of wells; and

(b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, wherein said plurality of projections is configured to be dipped from above into said wells, and wherein said second substrate is not a fiber optic array.

64. An array of arrays comprising:

(a) a first substrate with a surface comprising a plurality of wells; and

(b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents directly coupled thereto, and wherein said plurality of projections is configured to be dipped from above into said plurality of wells.

VII. THE AFFYMETRIX ARRAY PLATES AND ASSOCIATED PRODUCTS

65. Affymetrix markets and sells several products and instruments that are based on the 'array of arrays' for the parallel analysis of samples and that infringe the '841 and '020 patents. Most of the information about the accused products that I have relied on is available from Affymetrix's 'Data Sheets', 'Package Inserts', and other product literature. I also have an

understanding of how the products work based on my experience and education. For example, Affymetrix has published the following 'Data Sheets': GeneChip HT PM Array Plate System for Human, Mouse, and Rat; GeneChip Human Genome U133 Arrays; GeneChip Mouse Genome Arrays; Data Sheet for the GeneChip Rat Genome 230 Arrays; "Axiom Genotyping Solution"; 3' IVT Array Strips for Human, Mouse, and Rat; GeneTitan Instrument for Automated Array Processing; "Automated array processing with the GeneTitan family of instruments"; GeneAtlas Personal Microarray System; GeneChip HT Array Plate Scanner; GeneChip 3' IVT Express Kit and GeneChip HT 3' IVT Express Kit. Affymetrix has published the following 'Package Inserts': HT MG-430 PM Array Plate; GeneChip HT RG-230 PM Array Plate; Human Genome U219 Array Plate; Axiom Genome-Wide Human Array Plate; Axiom Genome-Wide ASI 1 Array Plate; Human Gene 1.1 ST Array Plate; Mouse Gene 1.1 ST Array Plate; Rat Gene 1.1 ST Array Plate; Human Genome U219 Array Strip; MG-430 PM Array Strip; RG-230 PM Array Strip; GeneTitan Hybridization, Wash, and Stain Kit for 3' IVT Arrays; GeneChip HT 3' IVT Express Kit; Axiom Genome-Wide Human Reagent Kit; and GeneChip WT Terminal Labeling Kit; GeneTitan Hybridization, Wash, and Stain Kit for WT Array Plates; and GeneTitan Wash Buffer A and B Module. Where I relied on materials in addition to these 'Data Sheets' and 'Package Inserts', I make specific reference to such materials below.

66. Affymetrix markets and sells a number of different types of array plates:

- The HT PM Array Plates for Human, Mouse, and Rat – the GeneChip HT HG-U133+ PM Array Plate; the GeneChip HT MG-430 PM Array Plate; the GeneChip HT Rat Focus Array Plate, the GeneChip HT Human Genome U133A/U133B Array Plate Set, the GeneChip HT Mouse Genome 430A/430B Array Plate Set, and the GeneChip HT RG-230 PM Array Plate.

The GeneChip HT MG-430 PM Array Plate and the GeneChip HT RG-230 PM Array Plate are available in 16-, 24-, and 96- array plate configurations. The GeneChip HT Rat Focus Array Plate, GeneChip HT Human Genome U133A/U133B Array Plate Set, and GeneChip HT Mouse Genome 430A/430B Array Plate Set are available in 24-, and 96- array plate configurations.

- The Human Genome U219 Array Plate. This array plate is available in 96-array plate configuration.
- The 1.1 ST Array Plates – the Human Gene 1.1 ST Array Plate, the Mouse Gene 1.1 ST Array Plate, and the Rat Gene 1.1 ST Array Plate. These array plates are available in 16-, 24-, and 96- array plate configurations.
- The Axiom Array Plates - the Axiom Genome-Wide Human Array Plate, and the Axiom Genome-Wide ASI 1 Array Plate. These array plates are available in 24- and 96-array plate configurations.
- The 3' IVT Array Strips for Human, Mouse, and Rat – the HG-U219 Array Strip; the MG-430 Array Strip; and the RG-230 Array Strip. These array strips are available in 4-array strip configuration.

All of these array plates and strips are used for gene expression analysis with the exception of the Axiom Array Plates, which are used for genotyping analysis. Unless specifically noted, I will refer to all of these array plates and strips collectively as the 'Accused Array Plates', 'Accused Array Strips', or 'Accused Array Plates and Strips'.

67. Affymetrix markets and sells a number of instruments for the processing and analysis of the Accused Array Plates and Strips. Such instruments include the GeneTitan Instrument, the

GeneTitan Multi-Channel Instrument, the GeneAtlas, the GeneChip Array Station and the GeneChip HT Array Plate Scanner. Unless specifically noted, I will refer to all of these instruments collectively as the 'Accused Instruments'. I sometimes refer to the instruments capable of imaging (the GeneTitan Instrument, the GeneTitan Multi-Channel Instrument, the GeneAtlas Instrument, and the GeneChip HT Array Plate Scanner) as the 'Accused Scanning Instruments'. The Accused Instruments are described further below, but differ primarily in the number of steps that they perform in an automated mode, the rate at which they can perform analyses and the number of arrays that they are formatted to handle, but otherwise perform the analyses using a common protocol.

68. The Accused Array Plates and Strips also require the use of kits that contain various components required to carry out the assays. The Human Genome U219 Array Plate is used with the HT 3' IVT Express Kit and GeneChip/GeneTitan HT Hybridization, Wash and Stain Kit. The HT Array Plates (HT HG-U133+ PM Array Plate, HT MG-430 PM Array Plate, HT RG-230 PM Array Plate, U-133 Array Plate Set and 430 Array Plate Set) are used with GeneChip HT 3' IVT Express Kit and GeneTitan Hybridization, Wash and Stain Kit. The 1.1 ST Array Plates are used with the GeneChip WT Terminal Labeling and Control Kit and the GeneTitan Hybridization, Wash and Stain Kit. The Axiom Array Plates are used with the Axiom Genome-Wide Human Reagent Kit. The 3' IVT Array Strips are used with the GeneAtlas Hybridization, Wash and Stain Kit and the 3' IVT Express Kit. Unless specifically noted, I will refer to all of these kits as the 'Accused Kits'. The Accused Kits are necessary to conduct the assays marketed by Affymetrix. The kits include, for example, the buffers and bead reagents used to isolate RNA from a biological sample, the buffers and reagents needed to prepare target analytes prior to hybridization to the array, the buffers and reagents (including biotin-modified reagents) used to label the target analytes, and hybridization controls used to ensure that the experiments are valid.

69. In many instances below, I will refer to the Accused Array Plates and Strips, the Accused Instruments, and the Accused Kits collectively as the 'Accused Products'.

70. The GeneAtlas instrument is designed to offer low throughput users a convenient and integrated product for performing whole genome analyses of complex biological samples. The instrument includes a hybridization station, a fluidics station and an imaging station and requires the user to manually perform steps to move samples between the stations. The GeneAtlas is used with the Accused Array Strips. The GeneAtlas uses an array plate that presents four identical arrays that are arranged in a linear strip. Each array is positioned on the end of a projection and the array strip is designed to be inserted into a complementary sample plate, or first substrate, that has individual samples in each of four sample wells. The array strip is designed to be used with a four-well microtiter plate.

71. The GeneTitan Instruments provide a hands-free, automated solution for monitoring gene expression and genome-wide SNP genotyping and are intended for laboratories that perform medium to high throughput analyses. The GeneTitan Instrument and the GeneTitan Multi-Channel (MC) Instrument automate array processing by combining a hybridization oven, fluidics processing, and imaging device into a single bench-top instrument. The imaging device in the GeneTitan MC Instrument uses an external, high-intensity xenon lamp and dual excitation and emission filters to capture images from array plates for use in genome-wide expression and genotyping studies. The imaging device in the single-channel GeneTitan Instrument uses an internal LED and a single emission filter to acquire data from expression array plates for genome-wide expression profiling. Both instruments use an array plate that presents 96 sample wells that are arranged in the standard 8x12 microtiter plate format. The instruments are designed to perform an automated analysis of individual samples that are each contained in separate wells. For each sample, the oligonucleotide

array is used to detect the presence or absence of different target analytes. The GeneTitan Instrument is used with all of the Accused Array Plates with the exception of the Axiom Array Plates, which are used with the GeneTitan Multi-Channel Instrument.

72. The GeneChip Array Station is a robotic system that is marketed by Affymetrix to automate many of the labor-intensive tasks required when preparing mRNA samples for gene expression analysis. The array station automates the hybridization of target to the Accused Array Plates, performs washing protocols on the plate, and performs the staining protocol of the plate prior to scanning. The GeneChip Array Station is designed to be used with standardized 96 well microtiter plates.

73. The GeneChip HT Array Plate Scanner is marketed by Affymetrix to scan and create high resolution images for all Accused Array Plate products and applications. The scanner uses a high-intensity LED excitation source, auto-focus optics and a CCD camera to provide high throughput analysis of the Accused Array Plate products. The instrument requires that the user insert samples for analysis. The Accused Array Plates must be processed to introduce a label onto the target analytes and Affymetrix offers reagents for this purpose.

VIII. USE OF THE ACCUSED PRODUCTS INFRINGES THE '841 PATENT

74. All of the claims of the '841 patent are method claims. I have been advised that to infringe a method claim, there must be a user who practices all of the steps of the method. In the case of the Accused Products, I have been asked to determine whether a user of the Accused Products infringes the asserted claims. Examples of users may include (i) Affymetrix employees using the Accused Products during the development process; (ii) Affymetrix employees using the Accused Products in the course of Affymetrix's scientific services programs; or (iii) end customers. In the last example, I understand that Affymetrix is nonetheless liable for infringement if it induces

or contributes to the use of its products in an infringing manner. The Affymetrix literature does just that by instructing the end user to use the Accused Products in a manner that infringes the claims, as more specifically described below.

75. Claim 1 of the '841 patent recites 'A method of detecting the presence or absence of a plurality of different target analytes'. The Accused Products detect the presence or absence of a plurality of different target analytes as more specifically described below.

76. Claim 1 recites "(a) providing a first substrate with a surface comprising a plurality of assay wells, wherein said assay wells contain sample solutions each having a plurality of different target analytes;". The Accused Products perform this step.[1] The individual sample solutions are placed into a plate that contains separate wells, such that each well contains a single sample, each having a plurality of different target analytes. The microtiter plate is the 'first substrate'. The samples plates are described in technical support documentation provided by Affymetrix as well as in many non-public documents prepared by Affymetrix. Each sample will typically contain many different target analytes that can be detected to determine whether each is present or absent in the sample. Depending on which instrument is used and what format is employed, the number of samples that are analyzed can be greater or less than 96.

77. Claim 1 recites "(b) providing a second substrate comprising a plurality of array locations, each array location comprising a plurality of discrete sites on a projection, wherein said sites comprise different bioactive agents;". The Court interpreted the term 'second substrate' to mean 'a material that can be modified to contain discrete individual sites appropriate for the

[1] It does not appear that the Court construed the term 'first substrate' to have the same meaning as the term 'second substrate'. Even if it had, a microtiter plate could be modified to contain discrete individual sites appropriate for the association or attachment of beads, and the patents-in-suit disclose embodiments that are modified in this way. See '841 patent figure 1D. Thus, the Affymetrix products meet this limitation under either interpretation.

attachment or association of beads and is amenable to at least one detection method', but the Court stated that the invention is not limited to embodiments that use beads. The Accused Products have a second substrate that presents multiple copies of an oligonucleotide array, and which is known as the 'Array Plate' or the 'Array Strip'. Each individual array is presented on the end of a projection, or peg, on the substrate. In the Affymetrix Accused Array Plates and Strips, the substrate is made of glass. See AFMX0612203-612356. The glass in the Affymetrix product is 'a material that can be modified to contain discrete individual sites appropriate for the attachment or association of beads and is amenable to at least one detection method'. The '841 patent identifies glass as a substrate that can be used in the invention (col. 7, line 38). Further, the second substrate has a plurality of pegs and a peg is a 'location' for purposes of claim 1. In addition, I am aware of numerous methods for attaching or associating beads to surfaces like the glass surface of the Affymetrix substrate. For example, one could use various adhesives, surface chemistries, surface etchings, or binding ligands (see '841 patent, col. 9, lines 45-48) to attach or associate beads. The bioactive agents are, in the most common applications, oligonucleotide molecules. The oligonucleotides in the Affymetrix products could be attached to microspheres; indeed, they could be synthesized directly onto the surface of a bead. Thus, although the Affymetrix substrate does not include beads, it could be modified to include beads. Because it is made of glass and because the use of beads is unnecessary in the Affymetrix products, the Affymetrix glass is at a minimum equivalent to glass that can be modified to include beads. The arrays that are present on the second substrate can either be identical or different, depending on the application.

78. The array is prepared using a photolithographic process to prepare a plurality of discrete sites wherein the sites comprise distinct, and usually different, bioactive agents. The Court construed the term 'discrete sites' to mean 'sites that do not touch another site'. The Affymetrix

arrays contain sites that do not touch other sites. For example, two adjacent regions or 'features' are modified with different oligonucleotide probes. The compositions of the centers of these two features are distinct from one another and from the composition of the substrate at a position midway between the two centers and therefore represents discrete sites. See Goldberg Deposition, pp. 180-183. Further, 'advanced image processing and data analysis software and algorithms' are used to analyze the feature to detect the presence or absence of target analytes. See Goldberg Deposition, p. 172. Therefore, I infer that the composition of the substrate at the region midpoint between two adjacent features has an insignificant impact on the data that is acquired by the instrument. The center regions of adjacent features are thus 'discrete sites' that do not touch each other. In addition, even if the entire feature is considered the site, the Affymetrix arrays contain a plurality (i.e., more than one) of features which do not touch other sites. For example, non-adjacent features do not touch each other, and would be considered discrete sites.

79. Even if entire adjacent features are considered to be the sites, then the Affymetrix product would still meet the 'discrete sites' limitation under the doctrine of equivalents, as I understand it, for the following reasons. First, as explained, whether the sites touch other sites has no bearing on the ability to detect the presence or absence of target analytes according to claim 1. The Scanning Instrument and data analysis protocols effectively ignore the portion of the features that might touch and focuses instead on the center regions of the features for analysis. Thus, whether the features are touching (instead of being separated by a small gap) is a minor distinction that adds nothing of significance. Second, a feature that touches an adjacent feature performs substantially the same function, in substantially the same way to achieve substantially the same result as one that does not touch an adjacent feature. The Affymetrix 'sites' perform the same function as the 'discrete sites' in the patent claims because they are intended to detect the presence or absence of target

analytes. The Affymetrix 'sites' perform this function in substantially the same way because they represent distinct patches that can be distinguished from other patches using the Accused Scanning Instruments. Hence, the Affymetrix 'sites' achieve the same results as the 'discrete sites' in the patent claims because they allow the detection of a plurality of target analytes in a sample. Third, at the time of the invention the use of photolithographic processes and the use of beads were known alternative ways to generate the arrays. The spacing of features using photolithography was well known, and it was well known to those in the art that features could alternatively be spaced such that they were far apart or close together or even overlapping. These spacings were known to be equivalent for purposes of detecting the presence or absence of target analytes, and therefore were a matter of design choice.

80. Claim 1 recites "(c) dipping the projections of said second substrate into said assay wells such that each array location of said second substrate contacts sample solution in a different well of said first substrate under conditions suitable for binding of said different target analytes to said different bioactive agents, thereby processing said sample solutions in parallel;". The Accused Products perform this step. To perform an analysis, the Accused Array Plates and Strips are placed into the sample plate such that each peg and associated array of the Array Plate is inserted into a sample that is present within a single well of the sample plate. The Accused Instruments maintain conditions that are suitable for the hybridization of analytes in the sample with oligonucleotides within the array. Affymetrix provides reagents (the Accused Kits) that ensure solution conditions that are appropriate for hybridization and the instrument maintains adequate control over temperature and hybridization time to ensure suitable hybridization. The hybridization conditions are selected to ensure efficient hybridization between a target analyte and a probe strand that has a matched, or

complementary, sequence with respect to the former. Under these same conditions, combinations of probe strand and target analyte that are not perfectly complementary will not appreciably hybridize. In this way, the array of arrays allows many different samples to be analyzed in parallel such that each sample is analyzed for the presence or absence of many target analytes.

81. Claim 1 recites "(d) detecting the presence or absence of said target analytes". The Affymetrix products perform this step. Following an incubation during which the hybridization is allowed to proceed, the array plates are washed, treated to introduce labels onto the target analytes and then scanned by the Accused Scanning Instruments to detect the presence or absence of the target analytes. The Accused Array Plates and Strips can be labeled in many different ways, including with enzyme activity, fluorescence, or binding of a secondary antibody. A common format relies on using target analytes that are prepared so that they contain the biotin molecule. After the target strands are hybridized to probe strands within the array, they are labeled through a binding reaction with streptavidin-phycoerythrin. The array is then scanned by the instrument to quantitate the amount of phycoerythrin label in each site of the array. Generally, the intensity of the optical signal that is measured from a site on the array is proportional to the amount of target analyte that is present in the sample. The instrument measures the intensity of the optical signal at each site in the array. Therefore, the method can measure the presence or absence of a large number of target analytes in the same sample.

82. Claim 2 recites "The method of claim 1, wherein said target analytes comprise nucleic acids or nucleic acid analogs". The Accused Instruments are commonly used to detect nucleic acid analytes, such as DNA, in the sample or alternatively, nucleic acid analogs, such as RNA. In these applications, a target analyte can hybridize with an oligonucleotide at a site in the array. Under the conditions used in the instrument, hybridization is specific in that target DNA analytes will only bind

appreciably to oligonucleotides that have a complementary sequence. The target analyte comprises RNA in assays using the Accused Array Plates and Strips with the exception of the Axiom Array Plates, wherein the target analyte comprises DNA.

83. Claim 3 recites "The method of claim 2, wherein said nucleic acids comprise single nucleotide polymorphisms". Affymetrix markets the combination of the GeneTitan MC, the Axiom Array Plates, and associated kits to be used to analyze single nucleotide polymorphisms (SNPs) in a sample. SNPs represent conserved differences in the sequences of DNA amongst individuals and are important because they can be used to predict the onset of disease or other genetically-determined traits.

84. Claim 8 recites "The method of claim 1, wherein said array locations comprise from 100,000 to about 10,000,000 bioactive agents per square centimeter". Many of the Accused Array Plates and Strips have from 100,000 to 10,000,000 distinct bioactive agents per square centimeter. For example, the arrays that are used in the HT HG-U133+ PM Array Plate have approximately 1,300,000 sites and are each 8 microns in size, suggesting a total size for the array of approximately 9 mm by 9 mm, or approximately 1.56 million distinct oligonucleotides per square centimeter. The Axiom ASI 1 Plate and Axiom Genome-Wide Human Array Plate have a feature size of 5 microns, which would correspond to a density of approximately 4 million distinct oligonucleotides per square centimeter. See Axiom Genome-Wide ASI 1 Array Plate Package Insert and Axiom Genome-Wide Human Array Plate Package Insert. The 1.1 ST Human Gene Array Plate has a feature size of 5 microns. See Human Gene 1.1 ST Array Plate Package Insert. The 1.1 ST Mouse Gene Array Plate has a feature size of 5 microns. See Mouse Gene 1.1 ST Array Plate Package Insert. The 1.1 ST Rat GeneArray Plate has a feature size of 5 microns. See Rat Gene 1.1 ST Array Plate Package Insert. The Human Genome U219 Array Plate has a feature size of 8 microns. See Human Genome U219

Array Plate Package Insert. The Human Genome U133 Array Plate Set has a feature size of 8 microns. See GeneChip Human Genome U133 Arrays Data Sheet. The GeneChip HT MG-430 PM Array Plate has a feature size of 8 microns. See HT MG-430 PM Array Plate package insert. The Mouse Genome 430A/430B Array Plate Set has a feature size of 8 microns. See GeneChip Mouse Genome Arrays Data Sheet. The Human Genome U219 Array Strip has a feature size of 8 microns. See Affymetrix Human Genome U219 Array Strip Package Insert. The MG-430 PM Array Strip has a feature size of 8 microns. See Affymetrix MG-430 Array Strip Package Insert. The RG-230 PM Array Strip has a feature size of 8 microns. See Affymetrix RG-230 PM Array Strip Package Insert. An array that has a density of approximately 100,000 distinct oligonucleotides per square centimeter would correspond to a center-to-center spacing of adjacent sites of approximately 32 microns. Arrays that had feature sizes that were larger than this value, but smaller than 100 microns would infringe claim 9 of the ‘841 patent. Similarly, arrays that had a density of approximately 10 million distinct oligonucleotides per square centimeter would correspond to a center-to-center spacing of adjacent sites of approximately 3.2 microns. Arrays that had feature sizes that were smaller than this value, but greater than approximately 0.22 micron would infringe claim 7 of the ‘841 patent.

85. Claim 10 recites “The method of claim 1, wherein said bioactive agents are directly coupled to said array locations”. The Accused Array Plates and Strips are prepared using a photolithographic method. This method relies on the step-wise synthesis of oligonucleotide molecules directly on the substrate. The substrate is a glass slide that is modified with a hydroxyl-terminated silane layer that is then reacted with a oligo(ethylene glycol) linker that is terminated in a photoprotecting group. See AFMX1456815-1456925. Removal of this protecting group commences synthesis of the oligonucleotide. Hence, the resulting oligonucleotides are covalently, and therefore directly, coupled to the array locations of the substrate.

86. Claim 13 recites "The method of claim 1, wherein said target analyte is labeled". The Accused Array Plates and Strips that are used in gene expression analysis (all of the Accused Array Plates and Strips with the exception of the Axiom Array Platea) are treated prior to scanning so that the target analyte is labeled. Most commonly, the target analytes are prepared so that they are labeled with biotin molecules. Following hybridization of the target analytes to probes at sites in the array, the plate is treated with reagents (provided in the Accused Kits) that allow a streptavidin-phycoerythrin to bind to the biotin group. Additionally, an antibody directed against the streptavidin, and which may also be modified with a label, may bind to the target analyte. In this way, the target analyte is labeled prior to scanning. The GeneTitan MC instrument is used to analyze the Axiom Array Plates for applications in genotyping, particularly for the analysis of single nucleotide polymorphisms. In this application, the target analytes are not prepared to contain biotin molecules prior to hybridization with probes at sites in the array. Instead, following hybridization a labeled oligonucleotide is allowed to hybridize with the analyte and is then acted on by a ligase enzyme to covalently join it with the probe strand. See AFMX1451525-1451590. The oligonucleotide is covalently modified with a fluorescent label. The assay uses two oligonucleotides that differ in sequence at a single position and that are therefore able to distinguish between the two polymorphisms in the sample. Each of the two oligonucleotides is modified with different labels; that is, with labels that have different optical characteristics. The GeneTitan MC instrument is able to analyze each of the two labels separately and is therefore used to determine the relative amounts of the two labeled oligonucleotides that bind to the target analyte. This information is used to determine which polymorphisms are present in the sample.

87. Claim 14 recites "The method of claim 13, wherein said label comprises an optical label". In all cases, the Accused Scanning Instruments use optical scanners to analyze the array

plates and to detect an optically-active label that is associated with the target analyte which is bound to probe strands in the array.

88. Claim 15 recites "The method of claim 14, wherein said optical label comprises a fluorochrome". The kits that are marketed by Affymetrix most commonly use fluorescent labels, or fluorochromes, to detect target analytes on the array. Fluorescent labels are excited using light of an appropriate wavelength, after which they emit light at a slightly longer wavelength. The Accused Scanning Instruments detect the intensity of light at this latter wavelength that is emitted from each site in the array.

89. Claim 16 recites "The method of claim 1, wherein said detecting is done through the use of a change in optical signature". The Accused Scanning Instruments determine the presence or absence of target analytes by performing an optical scan of the array. The instruments use a photodetector to measure the optical signatures that correspond with the presence of a label at locations of the array. It is the differences, or changes, in the optical signature that correlate with the presence or absence of a target analyte at locations in the array.

90. Claim 17 recites "The method of claim 1, further comprising quantitating differences in concentrations of said target analytes". In many applications, it is important to obtain quantitative information about the concentrations of target analytes. The Accused Scanning Instruments provide a quantitative measurement of the optical signatures that correspond to the presence of labeled target analyte. Hence, the instruments are used to quantitate the differences in concentrations of the target analytes that are present in a sample. An example of the use of the arrays to quantitate differences in the concentrations of target analytes is the gene expression arrays. These arrays are used to measure the relative amounts of mRNA that are present in a cell and that approximately correlate with the levels of expression of each gene.

91. Claim 18 recites "The method of claim 17, further comprising quantitating a specific mRNA". All of the Accused Array Plates and Strips with the exception of the Axiom Array Plates are used for gene expression analysis. The use of these products entails a quantitative measure of the presence of specific mRNA molecules.

92. Claim 19 recites "The method of claim 18, comprising quantitating said specific mRNA in the presence of total cellular mRNA". The samples that are analyzed with the array plates are prepared using protocols that are intended to isolate the total complement of cellular mRNA molecules. Therefore, the instruments are used to perform assays that quantitate specific mRNA analytes that are present with the total cellular mRNA.

93. Claim 20 recites "The method of claim 1, wherein said assay wells comprise wells of a microtiter plate". The Accused Products use microtiter plates to provide the assay wells used to perform hybridization reactions.

94. Claim 21 recites "The method of claim 1, wherein said plurality of assay wells comprises 96 wells". All of the Accused Array Plates marketed by Affymetrix are designed to be used with 96-well microtiter plates. Array plates may have less than 96 pegs and associated array locations (as in the 16- and 24-array configurations) but are still formatted in a geometry that is compatible with the use of hybridization plates that have 96 wells.

95. Claim 24 recites "The method of claim 1, wherein optical signals generated at said discrete sites upon binding of said different target analytes to said different bioactive agents are detected". The Accused Products are used to analyze for the presence or absence of many target analytes that are present in the same sample. The ability to individually detect the target analytes follows from the use of an array that spatially resolves the individual assays. For example, following the hybridization reaction and labeling procedure, the Accused Scanning Instruments perform a scan

to detect optical signals associated with each site in the array. In this way, the instrument can detect the presence of many bioactive agents that are present in the sample.

96. Claim 25 recites "The method of claim 24, wherein said different target analytes comprise labels and wherein said optical signal occurs as a result of said labels recruited to said sites by said target analytes binding said different bioactive agents". The protocols that are used to label the target analytes are described in the discussion of claim 13 of the '841 patent. As that description makes clear, it is the hybridization of the target analyte with the probe strand in the array that recruits the label to the bioactive agent.

97. Claim 26 recites "The method of claim 24, wherein an enzyme generates species at said discrete sites that are optically detectable". The Axiom Array Plates use an enzyme to generate the species that are optically detected in the array plate. Specifically, following hybridization of the target analyte to a probe at a site in the array, a second labeled oligonucleotide is allowed to hybridize with the target analyte such that it is adjacent to the probe which is hybridized to the same target analyte. A ligase enzyme then acts on this structure to covalently join the probe and the labeled oligonucleotide to create a species that is optically detected by the instruments. See AFMX1451525-1451590.

IX. THE ACCUSED ARRAY PLATES AND STRIPS INFRINGE THE '020 PATENT

98. Unlike the '841 patent, all of the claims of the '020 patent are apparatus claims, which claim an 'array of arrays'. I have been advised that to infringe an apparatus claim, Affymetrix must make, use, sell, or offer to sell a product that contains each and every limitation of the claim. As discussed below, the Accused Array Plates and Strips include each and every limitation of the asserted claims of the '020 patent in a similar manner as the '841 patent. Many of the terms in the '020 patent claims are substantially the same as terms in the '841 patent. The discussion of those

terms above applies equally here and will not be repeated. Likewise, any discussion of terms in this section relating to the '020 patent also applies to the same term in the '841 patent section above.

99. The preamble of claim 1 is 'An array of arrays". Depending on the construction of the term 'array', each Affymetrix Accused Array Plate and Strip is an array of arrays. The Array Plates and Strips comprise a plurality of pegs, each of which represents a location having one array. Hence, the Array Plates and Strips have a number of individual arrays that is defined by the number of pegs on the substrate. Hence the plurality of arrays represents the array of arrays.

100. Claim 1 recites "(a) a first substrate with a surface comprising a plurality of assay wells comprising samples;" Affymetrix markets the Accused Array Plates and Strips as described earlier in this report. Affymetrix provides a microtiter plate with the Accused Array Plates and Strips. The microtiter plate is a substrate with a surface comprising a plurality of assay wells. The user places samples into the wells to perform the application.

101. Claim 1 recites "(b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and wherein said first substrate and said second substrate are arranged such that projections of said second substrate are fitted into assay wells of the first substrate" Each Accused Array Plate and Strip is a second substrate that comprises a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents. The Accused Array Plates and Strips commonly contain from 4 to 96 projections, each of which presents an array that contains a plurality of different bioactive agents. The sites within the array are discrete sites as described in the discussion of claim 1 of the '841 patent. The arrays that are present at the locations can either be identical or different, depending on the application. The pegs on the Accused Array

Plates and Strips are complementary to the wells of the assay plate such that projections of said second substrate are fitted into assay wells of the first substrate. The microtiter plate is positioned in a face-up orientation and the Accused Array Plate or Strip is configured to be inserted or dipped into the microtiter plate from above, such that each peg of the Accused Array Plate or Strip is inserted into a well of the microtiter plate that contains a sample.

102. Claim 3 recites "The array of arrays according to claim 1, wherein said assay wells comprise wells of a microtiter plate". Affymetrix provides hybridization trays that are microtiter plates.

103. Claim 4 recites "The array of arrays according to claim 3, comprising 96 wells". The Accused Array Plates come with hybridization trays that have 96 wells that are arranged in a 12 x 8 format.

104. Claim 7 recites "The array of arrays according to claim 1, wherein said bioactive agents are selected from the group consisting of nucleic acids, nucleic acid analogs, peptides, peptide structural analogs, saccharides, fatty acids, steroids, purines, and pyrimidines". The Accused Array Plates and Strips marketed by Affymetrix use nucleic acids as the bioactive agents.

105. Claim 9 recites "The array of arrays according to claim 1, wherein said array location comprises from 100,000 to about 10,000,000 bioactive agents per square centimeter". See discussion of claim 8 of the '841 patent.

106. Claim 11 recites "The array of arrays according to claim 1, wherein said bioactive agents are directly coupled to said array location". See discussion of claim 10 of the '841 patent.

107. Claim 16 recites "The array of arrays according to claim 1, wherein said second substrate comprises arrays made by photolithographic techniques". Affymetrix uses photolithographic techniques to create the arrays used in the preparation of the Array Plate products.

These techniques use a combination of photoprotecting groups and lithography masks to direct light to designated sites on a substrate to enable the synthesis of oligonucleotides at those sites. By performing a sequence of photodeprotection and nucleotide coupling reactions, oligonucleotides having designated sequences are synthesized at each site of the array.

108. Claim 18 recites "The array of arrays according to claim 1, wherein said bioactive agents comprise nucleic acids". See discussion of claim 7 of the '020 patent.

109. Claim 19 recites "The array of arrays according to claim 1, wherein said second substrate is not a fiber optic array". The Accused Array Plates and Strips that Affymetrix markets do not comprise a fiber optic array. The plates are prepared by first gluing individual arrays onto individual plastic pegs and then gluing the resulting pegs to a plate. See Goldberg Deposition, p. 101.

110. Claim 20 recites "An array of arrays comprising a plate having wells and a substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and wherein projections of said substrate are fitted into wells of said plate". See discussion of claim 1 of the '020 patent.

111. Claim 21 recites "The array of arrays according to claim 20, comprising 96 wells". See discussion of claim 4 of the '020 patent.

112. Claim 24 recites "The array of arrays according to claim 20, wherein said bioactive agents are selected from the group consisting of nucleic acids, nucleic acid analogs, peptides, peptide structural analogs, saccharides, fatty acids, steroids, purines, and pyrimidines". See discussion of claim 7 of the '020 patent.

113. Claim 26 recites "The array of arrays according to claim 20, wherein said array location comprises from 100,000 to about 10,000,000 bioactive agents per square centimeter". See discussion of claim 9 of the '020 patent.

114. Claim 28 recites "The array of arrays according to claim 20, wherein said bioactive agents are directly coupled to said array location". See discussion of claim 11 of the '020 patent.

115. Claim 33 recites "The array of arrays according to claim 20, wherein said second substrate comprises arrays made by photolithographic techniques". See discussion of claim 16 of the '020 patent.

116. Claim 34 recites "The array of arrays according to claim 20, wherein said bioactive agents comprise nucleic acids". See discussion of claim 18 of the '020 patent.

117. Claim 35 recites "The array of arrays according to claim 20, wherein said substrate is not a fiber optic array". See discussion of claim 19 of the '020 patent.

118. Claim 36 recites "An array of arrays comprising: (a) a first substrate with a surface comprising a plurality of wells; and (b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, and wherein projections of said second substrate are fitted into wells of the first substrate". See discussion of claim 1 of the '020 patent.

119. Claim 37 recites "The array of arrays according to claim 36, wherein said first substrate comprises 96 wells". See discussion of claim 4 of the '020 patent.

120. Claim 40 recites "The array of arrays according to claim 36, wherein said bioactive agents comprise nucleic acids". See discussion of claim 18 of the '020 patent.

121. Claim 42 recites "The array of arrays according to claim 36, wherein said array location comprises from 100,000 to about 10,000,000 bioactive agents per square centimeter". See discussion of claim 9 of the '020 patent.

122. Claim 44 recites "The array of arrays according to claim 36, wherein said bioactive agents are directly coupled to said array location". See discussion of claim 11 of the '020 patent.

123. Claim 49 recites "The array of arrays according to claim 36, wherein said second substrate comprises arrays made by photolithographic techniques". See discussion of claim 16 of the '020 patent.

124. Claim 50 recites "The array of arrays according to claim 36, wherein said second substrate is not a fiber optic array". See discussion of claim 19 of the '020 patent.

125. Claim 51 recites "An array of arrays comprising: (a) a first substrate with a surface comprising a plurality of wells; and (b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents, wherein said plurality of projections is configured to be dipped from above into said wells, and wherein said second substrate is not a fiber optic array". See discussion of claims 1 and 19 of the '020 patent.

126. Claim 52 recites "The array of arrays according to claim 51, wherein said first substrate comprises 96 wells". See discussion of claim 4 of the '020 patent.

127. Claim 55 recites "The array of arrays according to claim 51, wherein said bioactive agents comprise nucleic acids". See discussion of claim 18 of the '020 patent.

128. Claim 57 recites "The array of arrays according to claim 51, wherein said array location comprises from 100,000 to about 10,000,000 bioactive agents per square centimeter". See discussion of claim 9 of the '020 patent.

129. Claim 59 recites "The array of arrays according to claim 51, wherein said bioactive agents are directly coupled to said array location". See discussion of claim 11 of the '020 patent.

130. Claim 63 recites "The array of arrays according to claim 51, wherein said second substrate comprises arrays made by photolithographic techniques". See discussion of claim 16 of the '020 patent.

131. Claim 64 recites "An array of arrays comprising: (a) a first substrate with a surface comprising a plurality of wells; and (b) a second substrate comprising a plurality of projections, each projection comprising an array location, each array location comprising a plurality of discrete sites, wherein said sites comprise different bioactive agents directly coupled thereto, and wherein said plurality of projections is configured to be dipped from above into said plurality of wells". See discussion of claims 1 and 11 of the '020 patent.

132. Claim 66 recites "The array of arrays according to claim 64, wherein said first substrate comprises 96 wells". See discussion of claim 4 of the '020 patent.

133. Claim 69 recites "The array of arrays according to claim 64, wherein said bioactive agents comprise nucleic acids". See discussion of claim 18 of the '020 patent.

134. Claim 71 recites "The array of arrays according to claim 64, wherein said array location comprises from 100,000 to about 10,000,000 bioactive agents per square centimeter". See discussion of claim 9 of the '020 patent.

135. Claim 73 recites "The array of arrays according to claim 64, wherein said second substrate is not a fiber optic array". See discussion of claim 19 of the '020 patent.

136. Claim 76 recites "The array of arrays according to claim 64, wherein said second substrate comprises arrays made by photolithographic techniques". See discussion of claim 16 of the '020 patent.

137. I hereby certify under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Dated: August 2, 2010

Dr. Milan Mrksich

EXHIBIT A

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1994	Ph.D. in Organic Chemistry, California Institute of Technology, Pasadena, California

Research Experience and Positions:

1987-1989	Undergraduate Research Assistant with Professor Steven C. Zimmerman, University of Illinois at Urbana-Champaign, Illinois
1989-1994	Graduate Research Assistant with Professor Peter B. Dervan, California Institute of Technology, Pasadena, California
1994-1996	Postdoctoral Fellow with Professor George M. Whitesides, Harvard University, Cambridge, Massachusetts
1996-2000	Assistant Professor of Chemistry, The University of Chicago
1997-	Institute for Biophysical Dynamics, The University of Chicago
2000-2003	Associate Professor of Chemistry, The University of Chicago
2001-	Associate Director, Nanoscale Science and Engineering Center at Northwestern
2003-	Professor of Chemistry, The University of Chicago
2005-	Investigator, Howard Hughes Medical Institute
	Research Interests: Biomaterials and interfaces; Cell adhesion and migration; Electroactive interfaces; Physical organic chemistry of interfacial reactions; Bio-Inspired Nanostructured Materials; Biochips.

Honors:

1989	University of Illinois Marvel Undergraduate Research Award
1990-1993	National Institutes of Health National Research Service Award
1993-1994	Ralph M. Parsons Foundation Graduate Fellow
1994-1996	American Cancer Society Postdoctoral Fellow
1996-1999	Searle Scholar Award
1996-2001	Camille and Henry Dreyfus New Faculty Award
2000	Sloan Research Fellow
2000	Camille Dreyfus Teacher-Scholar Award
2000	Sara Jane Rhoads and Rebecca Raulins Lecturer, University of Wyoming
2002	TR100 Young Innovator Award
2002	R.C. Fuson Visiting Scholar, University of Illinois
2003	American Chemical Society Arthur C. Cope Young Scholar Award

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2005	Fellow, American Association for the Advancement of Science
2007	Murtiashaw Lecture, University of South Carolina
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Service and Advisory Positions:

1996-	DARPA Defense Sciences Research Council (2006-08, Chair)
1997-	Editorial Board of Langmuir
1998-2000	Scientific Advisory Board of Cellomics
1999-2007	Scientific Advisory Board of ChemoCentryx
1999-2005	Scientific Advisory Board of Surface Logix
2000-	Editorial Board of E-Biomed: The Journal of Regenerative Medicine
2000	WTEC Panel for International Evaluation of Tissue Engineering Programs
2001	Chair for NIH/BECON Symposium on Biosensors
2002-2007	National Institutes of Health BECM Study Section (2005-07, Chair)
2002	International Panel for Review of Materials Research in United Kingdom
2002	WTEC Panel for International Evaluation of Biosensor Programs
2002-2005	Board of Directors of the Pittsburgh Tissue Engineering Initiative, Inc.
2002-2003	Science and Technology Advisory Committee for Argonne National Laboratory
2003-2008	Board of Governors for Argonne National Laboratory
2003-2008	Scientific Advisory Board of Helicos
2004-	Editorial Board of IEEE Transactions on NanoBioscience
2004-	Editorial Board of Chemistry & Biology
2004-2007	Editorial Board of Chemical Society Reviews
2004-	Advisory Board of the Searle Scholars Program (2007-, Chair)
2005-	Founder and Scientific Advisory Board of WMR Biomedical, Inc.
2007-	Scientific Advisory Board of NanoInk, Inc.
2008-	Editorial Advisory Board of Small

Publications:

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Patents:

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EXHIBIT B

LIST OF MATERIALS REVIEWED AND/OR RELIED ON

The ’841 and ’020 patents and file histories

Defendant Affymetrix, Inc.’s Supplemental Response to Plaintiff’s First Set of Interrogatories (Nos. 3-5), dated October 31, 2009

Defendant Affymetrix, Inc.’s First Supplemental Response to Plaintiff Illumina, Inc.’s First Set of Interrogatories (Consolidated) (Nos. 1-3), dated March 26, 2010

Defendant Affymetrix, Inc.’s Supplemental Responses to Plaintiff’s First and Second Set of Interrogatories (Nos. 3-4, 11-12), dated June 14, 2010

Defendant Affymetrix, Inc.’s Second Supplemental Response to Plaintiff’s First Set of Interrogatories (09-655) (Nos. 1-2), dated June 14, 2010

Illumina, Inc.’s Supplemented Responses to Affymetrix, Inc.’s First Set of Interrogatories (Nos. 1-8), dated September 1, 2009, and exhibits thereto

Illumina, Inc.’s Responses to Affymetrix, Inc.’s Second Set of Interrogatories (Nos. 9-16), dated April 30, 2010, and exhibits thereto

Illumina, Inc.’s Opening Claim Construction Brief and supporting documents

Motion of Defendant Affymetrix, Inc. Requesting Claim Construction and Memorandum in Support and supporting documents

Illumina, Inc.’s Responsive Claim Construction Brief and supporting documents

Defendant Affymetrix, Inc.’s Responsive Claim Construction Brief

The Court’s Opinion and Order regarding claim construction, dated July 14, 2010

Deposition of Martin Goldberg, Ph.D., taken June 22, 2010, and exhibits thereto

“GeneTitan Instrument” – AFMX118742-1182746

“Falcon Screening Project: Genotyping Millions of SNPs across Thousands Samples Using ‘On Chip’ Ligation Assay” – AFMX1451525-1451590

“Automated Array Processing with the GeneTitan Family of Instruments” – AFMX0464291-464294

“Affymetrix corporate overview” – AFMX1314708-1314747

“Photolithographic Fabrication of High-Density Oligonucleotide Arrays: Challenges and Opportunities” – AFMX1323648-1323676

Powerpoint – AFMX1543565-1543710

“Lithography Overview” – AFMX0612203-612356

“Self-assembling monolayer chemistries for substrate functionalization and array synthesis” – AFMX1952149-1952190

“The Next-Generation of GeneChip Fabrication: Automated Oligonucleotide Synthesis Using New Process Chemistry and Silicon Substrates” – AFMX1549148-1549184

“Photolithographic Synthesis of Oligonucleotide Arrays” – AFMX1456815-1456925

Stenographic Transcript of Claims Construction Hearing, June 4, 2010

Illumina “Expression Profiling with BeadArray Technology” – ILL2938265-2938321

Data Sheet for the GeneChip HT PM Array Plate System for Human, Mouse, and Rat

Data Sheet for the GeneChip Human Genome U133 Arrays

Data Sheet for the GeneChip Mouse Genome Arrays

Data Sheet for the GeneChip Rat Genome 230 Arrays

Data Sheet: “Axiom Genotyping Solution”

Data Sheet for the Affymetrix 3’ IVT Array Strips for Human, Mouse, and Rat

Data Sheet for the GeneTitan Instrument for Automated Array Processing

Data Sheet: “Automated array processing with the GeneTitan family of instruments”

Data Sheet for the GeneAtlas Personal Microarray System

Data Sheet for the GeneChip HT Array Plate Scanner

Data Sheet for the GeneChip 3’ IVT Express Kit and GeneChip HT 3’ IVT Express Kit

Package Insert for the HT MG-430 PM Array Plate

Package Insert for the GeneChip HT RG-230 PM Array Plate

Package Insert for the Human Genome U219 Array Plate

Package Insert for the Axiom Genome-Wide Human Array Plate

Package Insert for the Axiom Genome-Wide ASI 1 Array Plate

Package Insert for the Human Gene 1.1 ST Array Plate

Package Insert for the Mouse Gene 1.1 ST Array Plate

Package Insert for the Rat Gene 1.1 ST Array Plate

Package Insert for the Human Genome U219 Array Strip

Package Insert for the MG-430 PM Array Strip

Package Insert for the RG-230 PM Array Strip

Package Insert for the GeneChip HT 3' IVT Express Kit

Package Insert for the GeneTitan Hybridization, Wash, and Stain Kit for 3' IVT Arrays

Package Insert for the GeneTitan Hybridization, Wash, and Stain Kit for WT Array Plates

Package Insert for the GeneAtlas Hybridization, Wash, and Stain Kit for 3' IVT Arrays

Package Insert for the Axiom Genome-Wide Human Reagent Kit

Package Insert for the GeneChip WT Terminal Labeling Kit

Package Insert for the GeneTitan Wash Buffer A and B Module

Site Preparation Guide for the Axiom Genome-Wide Human Assay

User Manual for the GeneChip HT 3' IVT Express Kit

Protocol for the Ambion WT Expression Kit

Protocol for DNA Labeling Reagent, DLR (Biotin-11-dXTP), Product No. 79015

Quick Reference Card for the Axiom Automated Target Prep Protocol

Quick Reference Card for the Axiom gDNA Sample Prep

Standardized Assays and Reagents for GeneChip Expression Analysis

GeneChip Expression Analysis Technical Manual for HT Array Plates Using the GeneChip Array Station

Technical Note: "Performance and Validation of GeneChip HT Human, Mouse and Rat PM Array Plates"

Affymetrix promotion announcing the Axiom Genotyping Solution

Affymetrix Q2 2009 Earnings Transcript